REMARKS

Reconsideration and withdrawal of the rejections of the application are respectfully requested in view of the amendments and remarks herewith, which place the application into condition for allowance.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 1-13 are now pending. Claims 1-4 are amended, without prejudice and new claims 5-13 are added without prejudice.

No new matter is added by this amendment.

It is submitted that these claims are patentably distinct from the prior art cited by the Examiner, and that these claims are in full compliance with the requirements of 35 U.S.C. §112. The amendments and remarks herein are not made for the purpose of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112; but rather the amendments and remarks are made simply for clarification and to round out the scope of protection to which Applicants are entitled. Support for the amended recitations in the claims and for the new claim is found throughout the specification and from the pending claims. More specifically, support for the amended recitation in claims 5 and 6 are found in the specification on page 3, lines 16-22.

II. OBJECTIONS TO THE SPECIFICATION

The specification was objected to for alleged informalities. The amendments to the specification render the objections moot.

Consequently, reconsideration and withdrawal of the objections to the specification are respectfully requested.

III. OBJECTIONS TO THE CLAIMS

Claims 1-4 were objected to for alleged informalities. The amendments to the claims render the objections moot.

Consequently, reconsideration and withdrawal of the objections to the claims are respectfully requested.

III. 35 U.S.C. §112, FIRST PARAGRAPH, REJECTIONS

Claims 1-4 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to convey that Applicants had possession of the claimed invention. The rejection is traversed.

The Examiner alleges that the claims, specifically claims 1 and 4, which are drawn to the use of an expression vector comprising the promoter construct, are genus claims because "they comprise three different elements . . . each of which constitute a genus: the isofunctional MPSV enhancer repeats, the isofunctionalIRF-1 binding sites, and the isofunctional CMV minimal promoter." (*Office Action*, at 4). As isofunctional variants are claimed for all three elements, the Examiner alleges that a person skilled in the art would reasonably conclude that the disclosure of the specification fails to provide a representative number of species to describe the genus and that applicants were not in the possession of the claimed genus. (*Office* Action at page 5-6). The rejection is respectfully traversed.

The recitation "isofunctional variants" meets the requirements of §112, first paragraph. The nucleotide sequence of the MPSV enhancer, the IRF-1 binding sites, and the CMV minimal promoter recited in claim 1 clearly provide a description of structure. Further, the function of the above elements are well-described in the specification. Specifically, the function of the MPSV

enhancer, the IRF-1 binding sites, and the CMV minimal promoter can be found in the paragraph beginning on page 7, line 7.

The term "isofunctional", derived from Greek means "the same function". Further, the specification provides that the "isofunctional" means having the same biological activity or function. (Page 7, lines 17-18). *Enzo Biochem Inc. v. Gen-Probe Inc.* (Fed. Cir. 01-1230; July 2002) holds that a functional description of genetic material may be sufficient to satisfy the written description requirement of 35 U.S.C. §112, since the requirement can be met by showing that invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics, including functional characteristics, when coupled with known or disclosed correlation between function and structure.

Applicants have clearly provided relevant, identifying structural characteristics in the form of the nucleotide sequence of the MPSV enhancer, the IRF-1 binding sites, and the CMV minimal promoter. Further, the specification demonstrates the functional properties of the above nucleic nucleotide sequences. In addition, the methods of using a known sequence to identify isofunctional variants were conventional in the art at the time of filing, as were the procedures to test promoter or enhancer activity. Therefore, the methods for testing promoter and enhancer activity as well as methods for binding of proteins to specific binding sites are well established in the art. There is no reason to expect that one of skill in the art could not identify a member of the claimed genus based on its structural and functional characteristics. Thus, Applicants had possession of the invention.

Furthermore, limiting the Applicants to only the nucleotide sequence of the MPSV enhancer, the IRF-1 binding sites, and the CMV minimal promoter would unduly narrow the

scope of the invention. Applicants had possession, at the time of filing, the full scope of the clamed invention. Limiting the invention as the Examiner proposes would be unjustifiable.

It is submitted that the claims are in compliance with the first paragraph of §112, and reconsideration and withdrawal of the rejections thereunder are requested.

IV 35 U.S.C. §112, SECOND PARAGRAPH, REJECTIONS

Claims 1-4 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. The rejection is traversed.

The amendments to the claims render the rejections moot. Moreover it is respectfully asserted that "fusion protein comprising IFR-1 and the estrogen receptor" does not render the claim indefinite. Indeed, the specification discloses the IFR-1-human estrogen receptor (hER). (Page 6, line 31-32). This receptor, abbreviated as hER throughout the entire application was used for the experiments disclosed in detail in Figures 1-13 and the corresponding pages in the specification. The specification supports a "fusion protein comprising IFR-1 and the estrogen receptor." (Page 6, lines 36). Therefore, the Examiner's assertion that "it appears from the specification . . . that the fusion protein is between IRF-1 and the hormone binding domain of the estrogen receptor . . ." is meritless. Further, as disclosed in Fig. 6 and the corresponding paragraph bridging pages 11 and 12, a fusion protein comprising IRF-1 and hER may also comprise additional elements, such as a green fluorescent protein, GFP. Thus, it is respectfully asserted that the element, "the fusion protein comprising IFR-1 and the estrogen receptor" as understood by a skilled artisan, does not render the instant invention indefinite.

Further, with respect to the recitation "suitable medium", all of the methods of culturing mammalian cells in media are known to a person skilled in the art. As an example of what is

meant by "suitable medium" one can refer to page 8 of the application. The methods of culturing mammalian cells in suitable media are quite standard and are well explained in the literature. One skilled in the art would know how the medium must be adapted in order for the specific mammalian cells to be cultured. Indeed, the Examiner admits that one skilled in the art is highly skilled. (*Office Action* at page 11). For example, rodent cells may need a different medium in comparison to human cells, or that primary cells prefer different conditions compared to established cell lines. A skilled artisan would know this. Therefore, the particular "suitable medium" should not need to be specified *ipsis verbis* in the claims or limited to the examples in the specification, as slight variations would still lead the skilled artisan to the invention.

Consequently, reconsideration and withdrawal of the Section 112, second paragraph, rejections are respectfully requested.

V. 35 U.S.C. § 103 REJECTIONS

Claims 1-4 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Kirchhoff et al., *Cytotechnology*, 1996, 22: 147-159 ("Kirchhoff"), in view of Von Hoegen et al. (WO 98/11241) ("Von Hoegen"). The rejection is traversed. The cited documents do not teach, suggest, or motivate a skilled artisan to practice the instantly claimed invention.

The instant invention is directed to, *inter alia*, a promoter-transactivator system for inducible high-level mammalian gene expression with the option of cell growth control comprising (a) a promoter construct (IRFE promoter) having the general structure: [MPSV-E]-[IRF-1-binding sites]-[CMV]—DNA; and (b) a transactivator construct coding for a fusion protein comprising IRF-1 and the estrogen receptor. Neither Kirchhoff nor Von Hoegen, either

alone or in combination, teach, suggest, disclose or motivate a skilled artisan to practice the instantly claimed invention.

The Examiner is respectfully reminded that for the Section 103 rejection to be proper, both the suggestion of the claimed invention and the expectation of success must be found in the prior art, and not Applicants' disclosure. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988).

Applying the law to the instant facts, Kirchhoff and Hoegen fail to teach or suggest the instantly claimed invention. Kirchhoff relates to regulation of cell growth by IRF-1 in BHK-21 cells. But one of ordinary skill in the art would not have motivated to combine Kirchhoff with von Hoegen because von Hoegen focuses on oligocistronic expression vectors. (See page 50, claim 1 and page 1, line 7). Oligocistronic expression vectors are highly specific expressions where two or more proteins are derived from one singular mRNA, and the control of expression mediated by the promoter/enhancer unit is one important factor. This is simply due to the fact that the oligocistronic mRNA must be *inter alia* stable and be produced in significant amounts. Further, such mRNA is generally longer than mRNA coding for one protein. Such oligocistronic mRNA further comprises additional elements for translation like IRES elements to which the ribosome attaches. Thus, the objective in von Hoegen is different than Kirchhoff.

One of ordinary skill in the art would recognize the known problems and drawbacks associated with oligocistronic expression. Thus, the person skilled in the art would not be motivated to combine the Kirchhoff and Von Hoegen documents.

Finally, it is also well-settled that "obvious to try" is <u>not</u> the standard upon which an obviousness rejection should be based. *See In re Fine.* And as "obvious to try" would be the

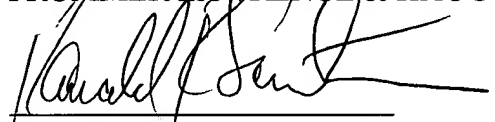
only standard that would lend the Section 103 rejection any viability, the rejection must fail as a matter of law.

Consequently, reconsideration and withdrawal of the Section 103 rejections are respectfully requested.

CONCLUSION

By this Amendment, the instant claims should be allowed; and this application is in condition for allowance. Favorable reconsideration of the application, withdrawal of the rejections, and prompt issuance of the Notice of Allowance are, therefore, all earnestly solicited.

Respectfully submitted,
FROMMER LAWRENCE & HAUG LLP

By: 

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